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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/764,110 12/06/96 CHEN

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EXAMINER
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HM12/0907

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NEW YORK NY 10017-5755

BERCH, M	
ART UNIT	PAPER NUMBER

1611

DATE MAILED:

09/07/99

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

**Advisory Action**Application No.  
**08/764,110**Applicant(s)  
**Chen**Examiner  
**Mark L. Berch**Group Art Unit  
**1611**

## THE PERIOD FOR RESPONSE: [check only a) or b)]

- a) ☒ expires 5 months from the mailing date of the final rejection.
- b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

- ☐ Appellant's Brief is due two months from the date of the Notice of Appeal filed on Aug 26, 1999 (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on Aug 26, 1999 has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

☒ The proposed amendment(s):

- ☐ will be entered upon filing of a Notice of Appeal and an Appeal Brief.
- ☒ will not be entered because:
- ☒ they raise new issues that would require further consideration and/or search. (See note below).
  - ☒ they raise the issue of new matter. (See note below).
  - ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
  - ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: See memo

- ☐ Applicant's response has overcome the following rejection(s):

- ☐ Newly proposed or amended claims \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.
- ☐ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
- ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
- ☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):
- Claims allowed: \_\_\_\_\_
- Claims objected to: \_\_\_\_\_
- Claims rejected: all
- ☐ The proposed drawing correction filed on \_\_\_\_\_ ☐ has ☐ has not been approved by the Examiner.
- ☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- ☒ Other Note PTO-1449

**MARK L. BERCH**  
PRIMARY EXAMINER  
ART UNIT 1611

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#### DETAILED ACTION

The amendment filed 8/26/99 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance and will not be entered because:

The proposed amendment raises new issues that would require further consideration and/or search.

A. The material added on page 2 is garbled. The first says, "at least one of D and E is nitrogen" but the second says "only one of D and E is nitrogen", which contradicts the "at least one". Suggested is saying "provided that the D-containing ring has exactly one nitrogen" which simply and clearly conveys applicants' intention.

B. The two additional choices added on page 4 lack description for reasons set forth below in the discussion of point 4. In some sense, it is even broader than what was there previously. For example, it now permits two substituents, that is, R<sup>5</sup> could be difluorophenyl; previously, only one was permitted.

C. Material has been deleted from the claims without brackets, so it is unclear whether this deletion was deliberate or accidental. For example, Page 4, line 4, the "pyrimidinyl" term (see previous page 5, line 3) has disappeared, three terms have disappeared from the R<sup>12</sup> definition, and there may be others as well.

In discussing the traverse of the previous rejection, the same numbering is used:

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1. In view of the two references supplied, this rejection is dropped.
2. The traverse is unpersuasive. The fact that fundamental research has established that certain disorders have a "nexus" to CRF antagonism does not mean that the term is definite. The problem is with the disorders for which this basic research has not been done. The procedure which needs to be followed, which was set forth previously on pages 3-5, constitutes undue experimentation. Language in other patents, which is based on different specifications and different claim language is not relevant.
3. The traverse is unpersuasive. The fact that there would have been an alternative way of describing an alkyl substituted with mercaptoalkyl does not mean that mercaptoalkyl could not have been meant. Further, the proposed "mercapto(C<sub>1</sub>-C<sub>7</sub> alkyl)" alternative would not amount to the same thing as a C<sub>1</sub>-C<sub>4</sub> alkyl substituted by mercapto(C<sub>1</sub>-C<sub>7</sub> alkyl), because mercapto(C<sub>1</sub>-C<sub>7</sub> alkyl) is broader. That is, mercapto(C<sub>1</sub>-C<sub>7</sub> alkyl) would permit the mercapto to be on the 1, 2, 3, or 4 position, whereas alkyl substituted by mercapto(C<sub>1</sub>-C<sub>3</sub> alkyl) would not permit such substitution.
4. The traverse is unpersuasive. Applicants state, "The examiner has ignored the language in the specification ... on page 9, lines 9-15." This is not so; the second half of page 6 of the remarks is devoted entirely to discussion of the material in the specification. Assuming that the deletions were intentional (see point C above), this is still broader than the specification states for reasons set forth previously. For example, as noted previously, a compound with R<sup>3</sup> as CN and R<sup>5</sup> as new material, e.g.

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fluorophenyl has now been added to the claim, yet such material is not on page 9. It should also be noted that page 9, line 12 is unclear, since the "which" of that line could be read as modifying just the pyrimidinyl, or all three rings. Applicants should also note that line 12 requires "more than two", whereas the claim language does not so require, permitting "two". Thus, a difluoropyrimidinyl, permitted by the new claim language, isn't really there on page 9.

5. The traverse is unpersuasive. It is correct that  $R^4$ , not  $R^5$  was intended here. Applicants' description of the page 9 material is not agreed with. It is describing a certain body of compounds, that are defined as set forth in that paragraph. Choices beyond what are specifically set forth in that paragraph are not there; that represents a later extrapolation.

6. If the deletion was intended, it would resolve this matter.

7. The amendment, if entered, would have resolved this point.

8. The traverse is unpersuasive. It is correct that this language was in original claim 17, but it is not in the specification as a use for the compounds. Of course, that material could be added back into the specification.

9. The traverse is unpersuasive. The inclusion of a specific inflammatory disease after the broad term raises the question of whether there is some unknown narrower meaning intended for the term, since otherwise there would be no need for the specific disease.

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10. The traverse is unpersuasive. As applicants correctly state, “an infection is not part of the regular functioning of the body”. Therefore an infection is not a disturbance in the function of the body, since it is not a part of the body function in the first place. Thus, an infection is no more a disorder than a tattoo or wearing a belt is a disorder, because these things are not in the category of the regular functions of the body. It is only the disturbances in those things which are disorders. As stated previously, it needs its own category.

11-12. If entered, the amendment would have resolved these points.

With regard to the improper Markush, see point A above.

The traverse on the scope of enablement rejection is unpersuasive. The proposed guidelines photocopy is noted, but that has to do with a 35 USC 101 rejection, which has not been made in this case. The examiner is not saying that a single compound cannot treat multiple disorders, only that the treatment of such a staggering list, is without precedent despite effort. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Fereus*, 163 USPQ 609. No such evidence has been presented in this case, and it was that lack of evidence which was fatal in *Feres*. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs Novo Nordisk*, 42 USPQ2nd 1001, 1006. Applicants’ discussion of Citron is not agreed with; the essential problem was not the lack of knowledge of the structure; method claims are

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routinely given for compounds of unknown structure, but rather because of the range of the use.

With regard to Fackelmann and Raloff, where specifically does it state that cancer can be treated generally? Indeed, where does the article even mention treating cancer at all? If treating cancer generally were simply a matter of reducing “psychological stress”, then cancer would long ago have been treated, since there are many methods, both pharmacological and non-pharmacological, to reducing stress. Langlois has a single appearance of the word “cancer”. No one reading that would assume that Langois was saying that cancers in general are treatable by melatonin antagonists. The indicated part of WO 99/11643 has been noted, but makes no reference at all to cancer. With regard to treatment of “chemical dependencies and addictions”, applicants cite REVIA. REVIA blocks the opiate receptor, a property that the claimed compounds are not alleged to have. Indeed, no one has ever succeeded in finding a treatment for opiate addiction without blocking the opiate receptor, and that alone is enough to be reason to doubt the efficacy of these compounds for the treatment of opiate addiction. The reference also cites one study showing effectiveness of REVIA for treatment of alcoholism. Alcohol addiction is somewhat atypical because unlike benzodiazepines, nicotine, etc, it does not involve a particular receptor. This one study hardly establishes efficacy, but even if it did, that would be exactly two, hardly evidence of a general effect. Addictions are in general one of the most difficult of all categories of pharmacological effects to achieve, evidence that the

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skill level in this art is low relative to difficulty of task. The treatment of addictions based on receptors without actually blocking the receptor has so far proved to be beyond the skill of practitioners in the art, and there is no reason to think that these compounds are capable of doing this. This is even more so for TRANXENE, which isn't alleged to treat alcohol addiction, but rather for providing for symptomatic relief of alcohol withdrawal, which is quite a different thing. Although applicants have removed AIDS from the claims, the same would apply to HIV infections. In Kinchington, it is assumed that page 91, not 99 was intended. If so, all it says is that three other categories "have been investigated." CFR antagonists were not mentioned, and just being investigated by itself does not mean they were effective. If they had been effective, the examiner believes that the review article would have mentioned it. Applicants then mention other references, none of which are alleged to say anything about HIV. With regard to stroke, the examiner's assertions are not "without supporting evidence", as Chalmers was cited for support on the top of page 12. The Kappelle abstract can hardly be said to support applicants' case, as it notes, "Several neuroprotective compounds have been studied, but at this moment [1997] none of these has definitely been proved effective." and "Treatment of acute ischemic stroke is uncertain." As for Owens, it supplies knowledge as of 1991. Such knowledge may or may not turn out to be incorrect as of filing date of this case, but what it does teach is hardly supportive, as was set out previously.



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Any inquiry concerning this communication or earlier communications from of Examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718.

A handwritten signature in black ink, appearing to read "Mark Berch". The signature is fluid and cursive, with the first name "Mark" and last name "Berch" clearly distinguishable.

Mark L. Berch

Primary Examiner

Group 1610 - Art Unit 1611

September 2, 1999